SAKAE CORPORATION
C/O ERIKA AMMIRATI   December 16, 2014
AMMIRATI REGULATORY CONSULTING
575 SHIRLYNN COURT
LOS ALTOS CA 94022

Re: K142789
    Trade/Device Name: A1c iGear System
    Regulation Number: 21 CFR 864.7470
    Regulation Name: Glycosylated hemoglobin assay
    Regulatory Class: II
    Product Code: LCP, JJE
    Dated: September 25, 2014
    Received: September 26, 2014

Dear Ms. Erika Ammirati:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

510(k) Number *(if known)*

Device Name
A1c iGear

Indications for Use *(Describe)*
The A1c iGear is intended for in vitro diagnostic use only for the quantitative measurement of the percent hemoglobin A1c (%HbA1c) from finger-stick blood or venous whole blood collected in either EDTA or sodium fluoride (NaF) for clinical laboratory and point of care use. The measurement of HbA1c is recommended to monitor long-term glycemic control of persons previously diagnosed with diabetes mellitus. This test is not for screening or diagnosis of diabetes.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D)   ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

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510(k) SUMMARY

The assigned 510(k) number is K142789.

(1): Name: Sakae Corporation
Address: 239 Onishi, Fujioka-shi, Gunma
370-1401 Japan

Phone: 011 81-274-52-3126
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Contact: Mr. Shinji Nakayama

Regulatory Contact: Erika Ammirati, Consultant to Sakae Corporation
Phone: 650-949-2768
FAX: 650-949-5347

Date: November 19, 2014

(2): Device name- trade name, common name, classification, product code

Trade name: A1c iGear System

Common Name: Glycosylated hemoglobin assay

Classification: Assay System: 21 CFR § 864.7470– Product code LCP, Class II
Analyzer: 21 CFR § 862.2160- Product code JJE, Class I

(3): Identification of the legally marketed predicate devices
A1c GEAR System, Sakae Corporation, Japan, K130014

(4): Device Description
A1c iGear is a fully automated, desktop, electrical spectrophotometer that measures %HbA1c in human whole blood using a dedicated reagent (MEDIDAS HbA1c). The system shines light from a 660 nm light emitting diode (LED) through the test material and measures the percent of hemoglobin A1c in the total hemoglobin (%HbA1c) based on the lot-specific reagent parameters and changes in light absorbency caused by antigen-antibody reactions.

MEDIDAS HbA1c (the reagent component) is composed of a test cartridge, capillary, pipette tip and master calibration card. The cartridge is pre-filled with the reagent; namely latex (Reagent 1: R1), antibody (Reagent 2: R2), and sample diluent solution. The A1c iGear and MEDIDAS HbA1c assay utilize an immuno-turbidimetric method to determine the percentage of HbA1c in total hemoglobin directly.

1st reaction: The hemolysate is mixed with the latex particles. Total hemoglobin and HbA1c have the same adsorption affinity for these particles, and therefore the percentage of HbA1c presented in the sample is proportional to latex-bound HbA1c.

2nd reaction: Addition of the antibody against human HbA1c creates a complex formed by the interaction between latex-bound HbA1c and the corresponding antibodies, which is agglutinated by goat anti-mouse IgG antibody. The amount of turbidity created by these aggregates is proportional to the amount of latex-bound HbA1c and therefore is proportional to the % of HbA1c in the total hemoglobin. A non-linear calibration curve is used to obtain the % of HbA1c in the total hemoglobin.

To perform with fingerstick or venous blood, the user collects the blood (1µL) into the supplied capillary. The capillary and the pipette tip are inserted into the cartridge, and the cartridge is placed into the analyzer. A1c iGear has the capacity to assay a total of three cartridges at one time. The measurement starts automatically when the ANALYZE button on A1c iGear is pressed. Upon starting the measurement, a lot-specific barcode on the cartridge is read, and the corresponding calibration information is used. The result(s) are displayed on the screen and printed out in 6 to 7 minutes. The HbA1c measurement range is 4.3-12.5%. Acceptable anticoagulants for venous blood samples include EDTA- 2K and sodium fluoride (NaF).

(5): Intended Use
The A1c iGear is intended for in vitro diagnostic use only for the quantitative measurement of the percent hemoglobin A1c (%HbA1c) from fingerstick blood or venous whole blood collected in either EDTA or sodium fluoride (NaF) for clinical laboratory and point of care use. The measurement of HbA1c is recommended to monitor long-term glycemic control of persons previously diagnosed with diabetes mellitus. This test is not for screening or diagnosis of diabetes.

(6): Technological Similarities and Differences to the Predicate

The following chart describes similarities and differences between A1c iGear and its predicate.

Manufacturer	SAKAE CORPORATION	SAKAE CORPORATION
Trade Name	A1c iGear with MEDIDAS HbA1c	A1c GEAR System (predicate device)
510(k) Number	K142789	K130014
Product Code	LCP	LCP
Regulation Number	864.7470	864.7470
Indications for use:	Quantitative measurement of percent hemoglobin A1c in human whole blood	Quantitative measurement of percent hemoglobin A1c in human whole blood
Methodology	Immuno-turbidimetric	Immuno-turbidimetric
Sample	Fingerstick blood or venous whole blood collected in EDTA-2K or sodium fluoride (NaF)	Fingerstick blood or venous whole blood collected in EDTA-2K or sodium fluoride (NaF)
Visual Display	Color LCD touch panel	LCD
Hemolysate preparation	Automatic	Automatic
Detection Method	Transmission	Transmission
Calibration	User; calibration card	User; calibration card
Recommended testing environment	Professional use; laboratory and point of care	Professional use; laboratory and point of care
Throughput	6-7 minutes per sample	6-7 minutes per sample
Analytical Range	4.3-12.5%	4.3-12.5%
Reagent Storage	2-8 degrees Celsius (36-46 degrees Fahrenheit)	2-8 degrees Celsius (36-46 degrees Fahrenheit)
Accuracy (Comparison)	Versus HPLC method $y=0.95x+0.11$, $R^2=0.99$, n=48	Versus HPLC method $y=0.99x+0.31$, $R^2=0.98$, n=40
Precision	Level 1: 5.6 %A1c, 3.5%CV, n = 40 Level 2: 7.3 %A1c, 1.2%CV, n = 40 Level 3: 10.7 %A1c, 2.4%CV, n = 40	Level 1: 5.5 %A1c, 1.1%CV, n = 80 Level 2: 11.1 %A1c, 1.4%CV, n = 80 Level 3: 12.1 %A1c, 1.5%CV, n = 80

The A1c iGear System is the same device as the A1c GEAR System previously cleared in K130014. The device has been modified to include a change in the name of the test system, the addition of an external connection to enable the analyzer to connect to external PC and USB flash memory, and simplification of the air filter and improvement of air circulation from the front side of the analyzer. Finally, electrical system improvements include: a color LCD touch panel and control, A/D converter, external communication, and operational board integrations. There was no change to the reagent component (MEDIDAS HbA1c cartridge).

(7): Performance Data

Precision with Control Material and Whole Blood
Three levels of control material and three whole blood samples targeted at low, middle and high levels of %HbA1c were each tested in duplicate for 10 days on each of two A1c iGear instruments for a total of 40 results per sample. The summarized data follow.

Precision Results with Control Materials and Whole Blood Samples

Test sample	# of iGear	# of test days	Mean (%A1c)	Repeatability		Between-Day		Between-iGear		Total Precision	
				SD	CV	SD	CV	SD	CV	SD	CV
Control L n = 40	2	10	5.9	0.06	0.93%	0.05	0.85%	0.02	0.34%	0.08	1.30%
Control M n = 40	2	10	7.4	0.08	1.04%	0.11	1.50%	0.00	0.00%	0.14	1.82%
Control H n = 40	2	10	11.7	0.10	0.87%	0.13	1.10%	0.09	0.75%	0.19	1.59%
Sample Low n = 40	2	10	5.6	0.06	1.02%	0.19	3.33%	0.00	0.00%	0.20	3.47%
Sample Middle n = 40	2	10	7.3	0.06	0.78%	0.03	0.37%	0.07	0.88%	0.09	1.24%
Sample High n = 40	2	10	10.7	0.09	0.83%	0.24	2.24%	0.05	0.45%	0.26	2.43%

Conclusions: All %CVs for repeatability were less than 3%, and all %CVs for total precision were less than 6%.

Precision Study-external

Studies for precision with control materials and whole blood, and a method comparison (accuracy), were performed at three external POC sites to evaluate the A1c iGear System in the POC setting. These evaluations also confirmed the usability of the modified instrument.

For the controls portion of the precision study, a 3-level control set was tested in duplicate for 20 days by each of three different operators at three separate sites. The results were analyzed by analysis of variance (ANOVA) under the assumption that the measurement results were independent with each other and followed a Gaussian distribution. Each variation was estimated as standard deviation (SD) and percent coefficient of variation (%CV). The results and the summarized statistics per sample (Table 1) and per site (Table 2) are shown below.

- Control L: Mean HbA1c = 5.9 % ± 0.12 %, CV 1.96 %
- Control M: Mean HbA1c = 7.4 % ± 0.11%, CV 1.42 %
- Control H: Mean HbA1c = 11.4 % ± 0.28 %, CV 2.42 %

Table 1 Summary of Control Precision Studies (for each sample, N=360)

Test sample	# of test days	Mean (%A1c)	Repeatability		Between-Day		Between-Operator		Between-Site		Reproducibility	
			SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
Control L	20	5.9	0.05	0.92%	0.06	1.01%	0.08	1.40%	0.00	0.00%	0.12	1.96%
Control M	20	7.4	0.06	0.81%	0.08	1.01%	0.02	0.24%	0.04	0.54%	0.11	1.42%
Control H	20	11.4	0.15	1.29%	0.15	1.31%	0.17	1.51%	0.05	0.46%	0.28	2.42%

Table 2 Summary of Control Precision Studies (for each site, N= 360)

Test sample	Site	# of test days	Mean (%A1c)	Repeatability		Between-Day		Between-Operator		Within-Site	
				SD	CV	SD	CV	SD	CV	SD	CV
Control L	A	20	5.9	0.07	1.12%	0.05	0.85%	0.00	0.00%	0.08	1.40%
	B	20	5.8	0.05	0.86%	0.03	0.57%	0.00	0.00%	0.06	1.03%
	C	20	5.9	0.05	0.77%	0.08	1.32%	0.03	0.48%	0.09	1.59%
Control M	A	20	7.5	0.06	0.85%	0.08	1.02%	0.00	0.00%	0.10	1.32%
	B	20	7.4	0.06	0.86%	0.04	0.54%	0.00	0.00%	0.07	1.01%
	C	20	7.4	0.06	0.76%	0.10	1.32%	0.03	0.38%	0.12	1.56%
Control H	A	20	11.6	0.09	0.74%	0.16	1.42%	0.00	0.00%	0.19	1.60%
	B	20	11.3	0.22	1.93%	0.12	1.03%	0.00	0.00%	0.25	2.19%
	C	20	11.4	0.09	0.80%	0.17	1.48%	0.06	0.55%	0.20	1.78%

For the whole blood portion of the precision study, sufficient venous whole blood was collected into EDTA-anticoagulated blood tube from three volunteers (inclusive of low, middle and high levels of %HbA1c) so as to provide each site sufficient test material necessary for 10-days of testing. The testing was performed two tests per day for each sample, for 10 days. Each whole blood set was run independently by three operators at the three separate sites. The results were analyzed by analysis of variance (ANOVA) under the assumption that the measurement results were independent with each other and followed a Gaussian distribution. Each variation was estimated as standard deviation (SD) and percent coefficient of variation (%CV). The results and the summarized statistics per sample (Table 3) and per site (Table 4) are shown below.

Table 3 Summary of Whole Blood Precision Studies (for each sample, n = 180)

Test sample	# of test days	Mean (%A1c)	Repeatability		Between-Day		Between-Operator		Between-Site		Reproducibility	
			SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
1	10	5.4	0.08	1.52%	0.08	1.54%	0.02	0.43%	0.03	0.54%	0.12	2.29%
2	10	7.2	0.08	1.06%	0.03	0.46%	0.00	0.00%	0.03	0.45%	0.09	1.24%
3	10	10.1	0.08	0.82%	0.12	1.17%	0.06	0.60%	0.06	0.63%	0.17	1.68%

Table 4 Summary of Whole Blood Precision Studies (for each site, n =180)

Test sample	Site	# of test days	Mean (% A1c)	Repeatability		Between-Day		Between-Operator		Within-Site	
				SD	CV	SD	CV	SD	CV	SD	CV
1	A	10	5.4	0.08	1.49%	0.07	1.30%	0.03	0.54%	0.11	2.04%
	B	10	5.3	0.05	0.99%	0.03	0.51%	0.04	0.79%	0.07	1.37%
	C	10	5.4	0.10	1.92%	0.12	2.27%	0.00	0.00%	0.16	2.98%
2	A	10	7.2	0.07	0.98%	0.03	0.47%	0.00	0.00%	0.08	1.09%
	B	10	7.2	0.08	1.07%	0.03	0.35%	0.01	0.10%	0.08	1.14%
	C	10	7.2	0.08	1.12%	0.04	0.52%	0.00	0.00%	0.09	1.23%
3	A	10	10.2	0.08	0.80%	0.07	0.66%	0.00	0.00%	0.11	1.03%
	B	10	10.0	0.09	0.90%	0.05	0.54%	0.04	0.37%	0.11	1.11%
	C	10	10.1	0.08	0.78%	0.19	1.84%	0.10	1.00%	0.23	2.23%

Conclusions: The imprecision, for both control material and whole blood, demonstrated %CVs of less than 3% across all variables.

Method Comparison Study-external
For the method comparison study, each site analyzed a minimum of 40 patient samples. Patient samples were representative of the validated range of the test system, capturing low, middle and high ranges. Matched whole blood samples and fingerstick samples were obtained from each individual (non-diabetic and diabetic) using standard technique. The fingerstick samples were analyzed by A1c iGear System by POC operators, and the EDTA samples were shipped to a reference laboratory that performed HPLC testing.

Linear regression analysis was performed where the A1c iGear results at each POC site (y-axis) were compared to the laboratory HPLC method (x-axis), and the slope, y-intercept, squared coefficient of correlation and bias were calculated. The results summary is shown in Table 5.

Table 5 Summary of Comparison Studies at 3 Sites-
All units %HbA1c (95% confidence intervals)

Study Site	n	Min	Max	Slope	y-intercept	R^2	Bias
1	42	5.2	11.3	0.95 (0.93 to 0.98)	0.10 (-0.13 to 0.32)	0.99	-0.25
2	44	5.1	11.7	0.95 (0.91 to 0.98)	0.20 (-0.03 to 0.44)	0.99	-0.18
3	40	5.2	9.3	0.94 (0.88 to 0.99)	0.34 (-0.02 to 0.70)	0.97	-0.09

Conclusions: The slopes, y-intercepts, and squared correlation coefficients were comparable across sites, and the values of the squared coefficients of correlation (R^2) were high (at least 0.97), indicating excellent correlation between A1c iGear System and the HPLC reference method. In addition, linear regression lines were nearly Y=X at each site, and biases were very small.

The following performance data were generated with the A1c GEAR analyzer, cleared under K130014. They are repeated here for completeness of the record.

Limit of Detection
The Limit of Blank (LoB) was determined by assaying 90 replicates of a zero sample (blank). The Limit of Detection (LoD) was determined by assaying 27 replicates of three low HbA1c samples. The LoB was determined to be 2.3% and the LoD was 2.6%.

Linearity
Linearity was evaluated according to CLSI-06A. The linearity was verified using two EDTA whole blood samples, including a normal sample with HbA1c concentration of 4.0% and an elevated HbA1c level sample with HbA1c concentration at 15.0%. The normal and high samples were inter-mixed to make a total of 11 intermediate samples covering the assay range. All intermediate dilutions were analyzed in replicates of three. The observed %HbA1c value for each intermediate dilution was plotted versus the expected analyte concentration. The linear regression is as follows: y=0.98x+0.19, r²=1.00.

Matrix Comparison

A study was performed using fingerstick whole blood, EDTA whole blood, and NaF whole blood. A total of 78 donor samples were collected from Site 1 using fingerstick and venous EDTA, 46 donor samples were collected from Site 2 using fingerstick and venous NaF, and 81 donor samples were collected from Site 3 using venous EDTA and NaF. Samples tested ranged from 4.3-10.9% HbA1c. The linear regression analyses are as follows:

Matrices	n	HbA1c%	Regression	r²
Fingerstick vs EDTA	78	4.3-9.0	y=0.96x+0.15	0.99
NaF vs. Fingerstick	46	4.8-8.8	y=1.04x-0.06	0.99
NaF vs. EDTA	81	5.3-10.9	y=1.01x+0.01	0.99

Interference and Analytical Specificity (variant hemoglobins)

An interference study was performed to assess common or known endogenous and exogenous substances that could interfere with the A1c Gear System. The potential interferents listed below were spiked into human EDTA and NaF whole blood samples with different levels of %HbA1c (~6.3% and ≥9.0% HbA1c). The %HbA1c values of the spiked samples were compared to reference samples (sample containing no interferent). Samples were tested in quadruplicate to give a total of four replicates per sample. The interferent study results are summarized in the table below:

Potential Interferent	Highest concentration in which no significant interference was observed.
Unconjugated Bilirubin	37 mg/dL
Triglycerides	2,000 mg/dL
Conjugated Bilirubin	40.4 mg/dL
Rheumatoid Factor	550 IU/mL
Acetaminophen	20 mg/dL
Ibuprofen	50 mg/dL
Glibenclamide	0.2 mg/dL
Metformin	5.1 mg/dL
Ascorbic Acid	6.0 mg/dL

Another interference study was performed to assess the effect of labile hemoglobin, carbamylated hemoglobin and acetylated hemoglobin with the A1c Gear System. Each modified hemoglobin was tested using EDTA and NaF whole blood samples with different levels of %HbA1c (~6.3% and > 9.0% HbA1c). Samples were incubated with the substance in parentheses below and analyzed for a total of four replicates per sample.

There was no significant interference with the following:
- Labile hemoglobin (D-glucose, up to 2000 mg/dL)
- Carbamylated hemoglobin (sodium cyanate, up to 10 mg/dL)
- Acetylated hemoglobin (acetylsalicylic acid, up to 200 mg/dL)

A hemoglobin variant study was performed using commercial samples known to contain hemoglobin variants C, D, E, S and F. Samples contained both low and high levels of % HbA1c at concentrations from 4.6-11.6% HbA1c. These variant samples were tested in duplicate. The results indicated samples containing Hemoglobin C were elevated by 24%, samples containing Hemoglobin D were elevated by 16%, samples containing Hemoglobin E were elevated by 13% and samples containing Hemoglobin S were elevated by 14%. Samples containing >10% Hemoglobin F were decreased by 32%. All variants tested were shown to interfere with this device.

The device labeling contains the following boxed warning:
"Hemoglobinopathies may interfere with glycated hemoglobin analysis. Samples containing the following hemoglobin variants have been shown to interfere with this assay: Hemoglobin C, Hemoglobin D, Hemoglobin E, Hemoglobin F (>10%) and Hemoglobin S."

Stability
The system kit (test cartridge) should be refrigerated at 2-8°C (36-46°F) and used immediately after opening. The expiration date of the Master Calibration Card and cartridge as stated on the package is 12 months after the date of manufacture.

Expected Values/Reference Range
The American Diabetes Association (ADA) expected value range is 4.0-6.0% HbA1c for people without diabetes. The ADA's most recent Clinical Practice Recommendation [1] for diabetes specified a treatment goal of less than 7% and suggests additional action when HbA1c level is above 8%.

HbA1c Value	Glycemic Goal
<8% HbA1c	Less stringent
<7% HbA1c	General (Non-Pregnant Adults)
<6.5% HbA1c	More stringent

[1] American Diabetes Association Standards of Medical Care in Diabetes 2014, 37 (Supplement1), S14-S80

Conclusions from Nonclinical and Clinical Testing
Nonclinical and clinical testing was performed for the A1c iGear System. The test system was shown to be safe and effective for its intended use.